



IARC - Multicenter Case-Control Study of ETS and Lung Cancer:

An Analysis:

Needs - Summary
Epi
Mechanism - genetic



Study characteristics:

- 12 centers; 7 european countries.
- 650 cases; 1542 controls
- Enrollment between 1988 and 1994
- Common questionnaire, (bar translation differences)
- Estimates of ETS exposure, Occupational exposure; Urban/Rural living; Education* and Diet*.
- Some inter-center & intra-country differences:
 - Response rate / selection of controls / age groups /
 - Diagnostic criteria

*Data on education and diet not available for all centers.

Results:



Reported source of ETS exposure:	No exposed (Cases/controls)	OR (95% CI)	Inter-center range:	Intra-country (G1:G2:G3) (I1;I2;I3)
Childhood:	389/1021	0.78* (0.64-0.96)	0.45-2.09	(0.60/0.82/0.55) (0.62/2.09/0.60)
Spousal:	344/700	1.16(n.s.) (0.93-1.44)	(<0.7 - >1.5)	-
Workplace	374/855	1.17(n.s) (0.94-1.51)	(8 cntrs >1.0)	-
Workplace or spousal:	527/1201	1.14(n.s) (0.88-1.47)	0.72-2.29	(0.88/1.22/2.01) (0.73/1.12/1.39)
Overall vehicles:	125/310	1.14(n.s) (0.88-1.48)	0 - 2.85	-
Overall public places:	174/454	1.03(n.s) (0.82-1.29)	0.24-2.32	-

* = Statistically significant. n.s = not statistically significant

Four largest ETS studies: (Spousal)

what about alk + coproven? see next page



Study/Year	Number of cases	OR (95% CI) Adjusted*	
IARC 1998	650	1.16 (0.93-1.44)	NS
Fontham 1994	651	1.29 (1.04-1.60)	Sig
Brownson 1992	431	1.00 (0.80-1.20)	NS
Wu-Williams 1990	417	0.70 (0.60-0.90)	NS

Combined meta-analysis (random effects) = 1.04 (0.81-1.33) *NS*

*Factors adjusted for, and method of adjustment vary by study

Workplace: Fontham cf IARC



	Unadjusted (crude) OR (95% CI)	Adjusted OR (95% CI)
IARC – Spousal	1.06 (0.87-1.30)	1.16 (0.93-1.44)
IARC – Workplace	1.09 (?)	1.17 (0.94-1.45)
Fontham – Spousal	1.26 (1.04-1.54)	1.29 (1.04-1.60)
Fontham – Workplace	1.12 (0.91-1.36)	1.39 (1.11-1.74)



Potential sources of Bias

- Selection bias / recall bias. %
- Diagnosis:
 - Histologically confirmed OR=1.11 (0.86-1.43)
 - Total (Sp or wkplace) OR=1.14 (0.88-1.47) > — % Δ
- Misclassification: %
- Confounding:
 - Accuracy of measurement
 - Residual confounding %
- Analysis (conditional versus unconditional) ? ~~ORnam~~ - %
- COMBINED EFFECT OF ALL BIASES ORnam
-

“Certainty” of the data



EITHER -

IARC - genetic susceptibility (1)



		AACR Meeting New Orleans March-April '98	Mol. Epi. Mtg Oslo, August '98	EACR Meeting Stockholm August '98
GSTM1 null genotype:	NS LC / S LC	1.25 (0.71-2.21)	1.0 (0.6-1.7)	-
	NS LC / Control	1.53 (0.87-2.69)	1.7 (0.7-4.1)	1.5 (0.9-2.7)
GSTT1 null genotype:	NS LC / S LC	1.82 (0.99-2.21)	0.7 (0.3-1.2)	-
	NS LC / Control	0.63 (0.34-1.16)	0.9 (0.3-2.3)	0.6 (0.3-1.2)
P53 mutations:	S LC / NS LC	2.7 (1.1-6.8)	2.1 (0.9-5.3)	2.7 (1.1-6.8)
	NS LC +ETS / NS LC -ETS	1.3 (0.2-8.0)	5.1 (0.8-3.1)	1.6 (0.3-7.6)
HPB-Hb adducts:	S/NS	-	P=0.01	P=0.01
	NS +ETS / NS -ETS	-	P=0.46	P=0.46

NS = Nonsmoker; S = Smoker; LC = Lung Cancer +/-ETS = with or without ETS exposure

OR:-

IARC Genetic Susceptibility



- **Polymorphisms of glutathione S-transferase M1 (OR=1.7; 95% CI 0.7-4.1) and glutathione S-transferase T1 (OR=0.9; 95% CI 0.3-2.3) are not predictive of lung cancer risk among non-smokers compared to non-smoking controls.**
- **Formation of haemoglobin adducts with 4-hydroxy-1-(3-pyridyl)-1-butanone (Hb-HPB), a metabolite of tobacco-specific nitrosamines, are not a valid marker of ETS exposure.**
- **Mutations in the p53 gene are more frequent in smokers (14/66) than in nonsmokers (10/88) and, in non-smokers, they are more frequent among cases exposed to ETS than among unexposed cases (OR 5.1; 95% CI 0.8-3.1).**
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P.Boffetta, P.Brennan, N.Malats, IARC, Lyon, On behalf of the International Study Group, and presented at the International conference on the clinical implications of Molecular epidemiology of Human Lung Cancer, August 9-12, 1988, Oslo, Norway.



IARC Genetic Susceptibility:

- OR (95% CI) for nonsmokers with lung cancer as compared to:

	Smokers with lung cancer	Nonsmoking controls
GSTM1 null genotype	1.0 (0.6-1.7) n.s.	1.7 (0.7-4.1) n.s.
GSTT1 null genotype	0.7 (0.3-1.2) n.s.	0.9 (0.3-2.3) n.s.
p53 gene mutations	0.5 (0.2-1.2) n.s.	-

- Tobacco-specific nitrosamine-derived (HPB) hemoglobin adducts (fmol/g globin):

Smokers:	26.3 ± 12.7	$\left. \right\}$	P= 0.01
Nonsmokers :	19.5 ± 7.9		
Nonsmokers with ETS:	20.4 ± 8.8		P=0.46
Nonsmokers without ETS:	18.8 ± 7.1		

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